Supplemental Table 1. Genetic variants in complement alternative pathway genes

# of Cases with Variant	Gene	Variant (GRCh37)	Transcript	Coding Change	Protein Change	gnomAD (v2.1.1) alt./total alleles (#homozygous alleles)	gnomAD (v2.1.1) Frequency in Sub-Populations	Functional Evidence	Final Classification using ACMG Criteria
2	*CFH*	1:196712596A>T	NM_000186.3	c.3148A>T	p.(Asn1050Tyr)	4155/282812 (40)	ALL:1.47% - AFR:2.74% - AMR:0.78% - ASJ:0.95% - EAS:0.0050% - SAS:0.72% - NFE:1.96% - FIN:0.86% - OTH:1.84%	NR	Likely benign
1	*CFHR1*	1:196799746C>G	NM_002113.2	c.724C>G	p.(Gln242Glu)	2305/264872 (617)	ALL:0.87% - AFR:8.94% - AMR:0.26% - EAS:1.98% - SAS:0.13% - NFE:0.019% - OTH:0.32%	NR	Benign
1	*CFHR4*	1:196882038A>T	NM_001201550.2	c.1166A>T	p.(Gln389Leu)	825/278922 (13)	ALL:0.30% - AFR:0.11% - AMR:0.12% - ASJ:0.18% - SAS:0.036% - NFE:0.55% - FIN:0.052% - OTH:0.31%	NR	Likely benign
1	*CFHR2*	1:196918738C>T	NM_005666.3	c.212C>T	p.(Thr71Met)	1124/282626 (9)	ALL:0.40% - AFR:0.072% - AMR:0.11% - ASJ:0.0096% - EAS:0.0050% - SAS:0.31% - NFE:0.63% - FIN:0.55% - OTH:0.32%	NR	Likely benign
1	*CFHR2*	1:196927185G>T	NM_005666.3	c.595G>T	p.(Glu199*)	2131/282428 (19)	ALL:0.75% - AFR:0.16% - AMR:0.15% - ASJ:0.029% - EAS:0.0050% - SAS:0.072% - NFE:0.95% - FIN:2.80% - OTH:1.08%	NR	Likely benign
1	*CFHR5*	1:196967354G>A	NM_030787.3	c.1067G>A	p.(Arg356His)	4559/280836 (55)	ALL:1.62% - AFR:0.52% - AMR:1.89% - ASJ:0.55% - SAS:0.28% - NFE:2.45% - FIN:1.32% - OTH:2.17%	NR	Likely benign
1	*CR2*	1:207641901A>G	NM_001877.4	c.475A>G	p.(Met159Val)	11/282706 (0)	ALL:0.0039% - AFR:0.0040% - AMR:0.0028% - EAS:0.0050% - SAS:0.026%	NR	VUS
1	*CR2*	1:207642523C>T	NM_001877.4	c.763C>T	p.(Arg255Trp)	2/31400 (0)	ALL:0.0064% - AFR:0.012% - NFE:0.0065%	NR	VUS

1	*CR1L*	1:207850900G>C	NM_175710.1	c.264G>C	p.(Lys88Asn)	585/280184 (4)	ALL:0.21% - AFR:0.0041% - AMR:0.020% - ASJ:0.13% - NFE:0.33% - FIN:0.47% - OTH:0.31%	NR	Likely benign
3	*CR1L*	1:207890892G>A	NM_175710.1	c.1498G>A	p.(Val500Ile)	12944/280448 (419)	ALL:4.62% - AFR:1.10% - AMR:2.56% - ASJ:2.30% - EAS:0.67% - SAS:5.93% - NFE:6.25% - FIN:4.98% - OTH:4.58%	NR	Likely benign
1	*CD46* (*MCP*)	1:207958446C>T	NM_002389.4	c.1058C>T	p.(Ala353Val)	4347/282180 (79)	ALL:1.54% - AFR:0.25% - AMR:0.19% - ASJ:0.77% - SAS:0.15% - NFE:1.96% - FIN:5.87% - OTH:1.32%	C3b and C4b binding slightly compromised. functional study (PMID: 16621965) -- similar enough to normal	Benign
1	*CFI*	4:110662159C>G	NM_000204.4	c.1642G>C	p.(Glu548Gln)	232/282678 (0)	ALL:0.082% - AFR:0.52% - AMR:0.17% - ASJ:0.0096% - NFE:0.026% - OTH:0.12%	NR	VUS
4	*CFB*	6:31914024T>A	NM_001710.5	c.26T>A	p.(Leu9His)	10656/277904 (250)	ALL:3.83% - AFR:1.18% - AMR:2.18% - ASJ:2.47% - EAS:1.80% - SAS:5.27% - NFE:4.56% - FIN:5.47% - OTH:3.87%	NR	Benign
1	*CFB*	6:31915614G>A	NM_001710.5	c.754G>A	p.(Gly252Ser)	6323/281672 (97)	ALL:2.24% - AFR:0.64% - AMR:1.32% - ASJ:1.32% - EAS:0.020% - SAS:0.21% - NFE:3.63% - FIN:2.50% - OTH:2.83%	NR	Benign
1	*CFB*	6:31918468A>C	NM_001710.5	c.1697A>C	p.(Glu566Ala)	2961/277960 (35)	ALL:1.07% - AFR:1.05% - AMR:0.95% - ASJ:2.12% - EAS:0.13% - SAS:2.52% - NFE:0.97% - FIN:0.056% - OTH:1.73%	NR	Benign
1	*C5*	9:123759929C>A	NM_001735.2	c.2686G>T	p.(Val896Leu)	11/251478 (0)	ALL:0.0044% - AMR:0.012% - NFE:0.0062%	NR	VUS
1	*C3AR1*	12:8211784A>G	NM_004054.3	c.998T>C	p.(Leu333Pro)	5759/282728 (82)	ALL:2.04% - AFR:0.38% - AMR:1.56% - ASJ:4.89% - EAS:0.0050% - SAS:0.78% - NFE:2.84% - FIN:1.97% - OTH:2.77%	NR	Benign

1	*C3*	19:6693026A>G	NM_000064.2	c.3299T>C	p.(Leu1100Pro)	5/28277 (0)	ALL:0.0018% - NFE:0.0039%	In silico protein modeling: predicted to destabilize an alpha helix fold (PMID: 26283675)	VUS
2	*C3*	19:6718146T>G	NM_000064.2	c.463A>C	p.(Lys155Gln)	765/282828 (2)	ALL:0.27% - AFR:0.032% - AMR:0.037% - ASJ:0.077% - NFE:0.54% - FIN:0.096% - OTH:0.26%	Recombinant expression studies: increased hemolytic activity (PMID: 30131807)	Likely benign
2	*THBD*	20:23028686C>A	NM_000361.2	c.1456G>T	p.(Asp486Tyr)	2115/276574 (60)	ALL:0.76% - AFR:0.037% - AMR:5.09% - EAS:1.16% - SAS:0.12% - NFE:0.022% - OTH:0.45%	NR	Benign

NR – not reported

Supplemental Table 2. Complement serology functional results

Complement component	Reference Intervals	PE n=25 Median (range)	Control n=25 Median (range)	P value
C1q function, U/mL	34-63	60 (34-71)	57 (47-65)	0.19
C2 function, U/mL	25-47	46 (33-59)	44 (34-51)	0.32
C3 function, U/mL	21-50	57 (34-70)	57 (45-64)	0.24
C4 function, U/mL	22-45	54 (32-67)	56 (46-61)	0.68
C5 function, U/mL	29-53	49 (36-64)	50 (41-57)	0.43
C6 function, U/mL	32-57	58 (34-71)	58 (45-64)	0.18
C7 function, U/mL	36-60	56 (45-66)	54 (47-59)	0.06
C8 function, U/mL	33-58	59 (38-69)	57 (47-63)	0.20
C9 function, U/mL	37-61	58 (42-69)	57 (48-62)	0.15

Median and range shown, comparison between cases and controls using Wilcoxon/Kruskal-Wallis Tests (Rank Sums)